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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,710	04/22/2005	Takeshi Ito	KUZ-0022	5270

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EXAMINER	
FOLEY, SHANON A	
ART UNIT	PAPER NUMBER
1619	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,710	ITO ET AL.	
	Examiner	Art Unit	
	SHANON A. FOLEY	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 8-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 8-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 8-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1 has been amended to include a negative proviso that the instant adhesive patch does not contain an organic acid salt. Support for this amendment is pointed to in the instant disclosure on page 1, line 15 to page 2, line 14. A review of the excerpt reveals that while there is a discussion of distinctions in prior art fentanyl patches comprising an organic acid salt, there is no indication that the instant composition claimed does not comprise an organic acid salt. In paragraph [0043] of the instant published disclosure, USPgPub 2007/0009588, some of the hydrophilic polymers listed are organic acid salts. These include carboxymethyl cellulose sodium, sodium polyacrylate and sodium alginate. Since the disclosure specifically teaches that inclusion of specific organic acid salts, the negative proviso now recited in claim 1 constitutes new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 8, 9, 11, 12, 14-16, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chono et al. (US 6,139,866), Tsuruda et al. (CA 2 424 579), Hirano et al. (US 6,495,159), Higo et al. (US 5,866,157) and Grond et al. (Clinical Pharmacokinetics. 2000; 38 (1): 59-89).

Chono et al. disclose an adhesive patch comprising a backing layer and a pressure-sensitive adhesive layer formed on one side thereof (col. 5, lines 39-43), wherein the pressure-sensitive adhesive layer comprises a pressure-sensitive adhesive base (col. 5, lines 19-22). The inclusion of a percutaneous absorption enhancer in the pressure-sensitive adhesive layer is one or more selected from a group consisting of isopropyl myristate and oleyl alcohol (col. 4, lines 6-8, 22-23). Chono et al. disclose fentanyl as an active ingredient in the concentration of 5% by weight, see Example 6. Chono et al. further teach the inclusion of a tackifier, Arcon P-100, see col. 3, lines 44-53. It is well known in the art that Arcon P-100 is an alicyclic saturated hydrocarbon resin, as evidenced by Higo et al. (Example 2). The pressure-sensitive adhesive base of Chono et al. comprises polyisobutylene and a styrene/isoprene/styrene block copolymer. Chono et al. discloses the weight ratio of polyisobutylene to styrene/isoprene/styrene is in the range of 1:1 and 1:4 (col. 3, lines 9-10), which encompasses the instant ratios. However, the

instant claims require that the PIB be between 8-15 wt %. Chono et al. fails to disclose these weight percent ranges.

However, Tsuruda et al. disclose an adhesive patch having combination of styrene/isoprene/styrene block copolymer and polyisobutylene (pg. 23, lines 20-24). Tsuruda et al. disclose the total amount of polyisobutylene be in the range of 1-20% by weight (pg. 21, lines 9-13). This range taught by Tsuruda et al. would include ranges between 8-15 wt %. Tsuruda et al. also teach that the amount of styrene/isoprene/styrene block copolymer being in the range of 15-30% by weight (pg. 20, lines 16-21).

From the teachings of Tsuruda et al., one of ordinary skill in the art at the time the invention was made would have chosen any particular combination of PIB and SIS within the ranges taught to arrive at a specific ration, including a 2:3 ration or a 3:2 ration, or any range between the two. It would have been an obvious design choice to one of ordinary skill in the art to modify the amount of the polymers, as desired, in order to adjust the adhesive strength and adhesion properties, as taught by Tsuruda et al. (pg. 23, line 10 - pg. 24, line 20). Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discover the optimum or working ranges involves only routine skill in the art (emphasis added). *In re Aller*, 105 USPQ 233. In the instant case, Chono et al. teaches that the instant ratios between PIB:SIS are 1:1, which teaches the ratios used in the instant examples 1-4 on page 20 of the instant disclosure. Regarding the obviousness of attaining ratios ranging from 2:3 and 3:2, as instantly recited, both Chono et al. and Tsuruda et al. teach varying ratios between PIB and SIS. Additionally, Tsuruda et al. teaches weight percentages of each ingredient that would have

rendered the ratio range instantly claimed prima facie obvious to one of ordinary skill in the art, absent unexpected results to the contrary.

In addition, Tsuruda et al. discloses an adhesive patch having a styrene/isoprene/styrene block copolymer and a combination of polyisobutylenes having high and low molecular weights, wherein the low molecular weight polyisobutylene is Vistanex LM-MH and the high molecular weight polyisobutylene is Vistanex MML-100 (pg. 21, lines 9-24; pg. 22, lines 10-12). It would have been obvious to one of ordinary skill in the art to utilize a combination of polyisobutylenes having high and low molecular weights in the adhesive patch of Chono et al. to improve adhesive strength, increase the length of time of adhesion to the to the skin and improve pain at the time of peeling, see page 22, lines 19-24 of Tsuruda et al.

Regarding the instantly required tackifier resin, Chono et al. disclose the tackifier resin being in the range from 5-50% by weight (col. 3, lines 56-60). Example 7 of Chono et al. demonstrates an adhesive patch of a similar composition having a tackifier resin at 32% by weight. It would have been obvious to one of ordinary skill in the art to modify the range of the tackifier resin, as desired, in order to regulate the viscosity and adhesive strength of the adhesive base, as taught by Tsuruda et al. (pg. 25, lines 9-25). Further, it has been held that where the general conditions of a claim are discloses in the prior art, discover the optimum or working ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Chono et al., Tsuruda et al. and Higo et al. do not teach a tackifier resin to be hydrogenated petroleum resin.

However, Hirano et al. teach an adhesive patch comprising a tackifier resin of hydrogenated petroleum resin, see column 6, lines 4-17.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the hydrogenated petroleum resin of Hirano et al. in the adhesive patch of Chono et al., Tsuruda et al. and Higo et al. since Hirano et al. specifically teach hydrogenated petroleum resin as a conventional alternative to Acron P-100™, see column 6, lines 4-17 of Hirano et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for using the hydrogenated petroleum resin of Hirano et al. in the adhesive patch of Chono et al., Tsuruda et al. and Higo et al. because Hirano et al. and Chono et al., Tsuruda et al. and Higo et al. teach that the tackifier resin as a component of a pressure sensitive adhesive that is used in an amount of no more than 50% weight of the adhesive patch, see column 6, lines 4-17 of Hirano et al. and column 3, lines 56-60 and Example 7 of Chono et al.

Regarding the newly recited limitation of the instant patch not containing an organic acid salt, Higo et al. teach that the inclusion of such salts cause irritation at the time of release and insufficient quantities of drug to be released, see column 2, lines 5-22.

One of ordinary skill in the art at the time the invention was made would have been motivated to eliminate an organic acid salt from the fentanyl patch formulation of Chono et al., Tsuruda et al., Hirano et al. and Higo et al. to reduce irritability and increase sufficient quantities of the drug. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for eliminating an organic acid salt from the patch of Chono et al., Tsuruda et al., Hirano et al. and Higo et al. since neither Tsuruda et al. nor Hirano et al. require an organic acid salt in the respective patch formulations, see Formulations 4, 5 and 7-10

of Tsuruda et al. bridging pages 35-39 and the working examples detailing the "Composition of the pressure-sensitive adhesive" bridging columns 8-16 as well as claims 1-12 of Hirano et al.

The instant claims have also been amended to require that the instant adhesive patch provides a long-term drug efficacy for more than 48 hours.

See the teachings of Chono et al., Tsuruda et al., Hirano et al. and Higo et al. above. None of the references discuss long-term efficacy of fentanyl for more than 48 hours. However, Grond et al. teach that transdermal therapeutic patches for fentanyl that provide drug efficacy for more than 48 hours, see the first two columns of 2.2 on page 64, Table 2 bridging pages 65-66, Figure 2 on page 67 and the first paragraph of section 2.5 on page 68.

One of ordinary skill in the art at the time the invention was made would have been motivated to provide fentanyl drug efficacy for at least 48 hours to provide relief from acute postoperative pain, chronic cancer pain and general chronic pain, see the first paragraph of section 4 on page 72 of Grond et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for administering an effective dose of fentanyl in a patch for at least 48 hours, as taught by Grond et al. in the patch of Chono et al., Tsuruda et al., Hirano et al. and Higo et al. since the parts required within the transdermal therapeutic system shown in Figure 1 on page 62 of Grond et al. are also required within the patch of Chono et al., Tsuruda et al., Hirano et al. and Higo et al.

Claims 4 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chono et al., Tsuruda et al., Higo et al., Hirano et al. and Grond et al. as applied to claims 1-3, 8, 9, 11, 12, 14-16, 19 and 20 above, and further in view of Urquhart et al. (US 4,031,894).

See the teachings of Chono et al., Tsuruda et al., Higo et al., Hirano et al. and Grond et al. above. None of the references teach the average molecular weight of the high molecular weight polyisobutylene as being in the range of 900,000-2,500,000. Nevertheless, it is well known in the art that Vistanex MML-100 has an average molecular weight about 1,200,000, as evidenced by Urquhart et al. (col. 6, lines 10-12), thus is in the range of 900,000-2,500,000.

Claims 5 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chono et al., Tsuruda et al., Higo et al., Hirano et al. and Grond et al. as applied to claims 1-3, 8, 9, 11, 12, 14-16, 19 and 20 above, and further in view of Scholz et al. (US 5,750,136).

See the teachings of Chono et al., Tsuruda et al., Higo et al., Hirano et al. and Grond et al. above. None of the references teach the average molecular weight of the low molecular weight polyisobutylene being in the range of 30,000 – 65,000. Nevertheless, it is well known in the art that Vistanex LMMH has an average molecular weight about 53,000, as evidenced by Scholz et al. (col. 6, lines 21-23), thus is in the range of 30,000 – 65,000.

Claims 10 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chono et al., Tsuruda et al., Higo et al. and Hirano et al. as applied to claims 1-3, 8, 9, 11, 12, 14-16, 19 and 20 above, and further in view of Zaffaroni (US 3,598,122) and Kochinke (US 5,350,581).

See the teachings of Chono et al., Tsuruda et al., Higo et al., Hirano et al. and Grond et al. above. None of the references teach the adhesive patch having an area of 10-75 cm^2. Zaffaroni discloses utilizing a transdermal bandage having a surface area of 0.5 to 400 cm^2, where the size is dependent on the activity of the drug and the rate of its absorption through the skin (col. 6, lines 25-29). It would have been an obvious design choice to one of ordinary skill in the art to modify the surface area of the adhesive patch in order to ensure that the amount of drug entering

the system appropriate for the treatment was safe and efficacious, as taught by Kochinke (US 5,350,581) (col. 1, lines 17-20) and Table 1 on page 62 and Table III on page 69 of Grond et al.

Response to Arguments

Applicant points out that Chono et al. only examines permeation rates out to 24 hours and argues that there is no reasonable expectation of success for maintaining long-term drug efficacy for more than 48 hours.

Applicant's arguments have been fully considered, but are found unpersuasive. The rejection relies on the combination of Chono et al., Tsuruda et al., Higo et al., Hirano et al. and Grond et al., rather than the teachings of Chono et al. alone. While the previously cited references do not evaluate the efficacy of fentanyl beyond a 24-hour period, Grond et al. teach that transdermal therapeutic patches for fentanyl that provide drug efficacy for more than 48 hours, see the first two columns of 2.2 on page 64, Table 2 bridging pages 65-66, Figure 2 on page 67 and the first paragraph of section 2.5 on page 68, demonstrating that fentanyl delivery via patch is efficacious for more than 48 hours.

Applicant discusses out the deficiencies of ion-pair adhesive patches requiring an organic acid salt and further points out that Chono et al. requires the organic acid salt, sodium acetate, in each of the formulations.

Applicant's arguments and a review of the references have been fully considered, but are found unpersuasive since Higo et al. discuss reasons for why the ordinary artisan would have been inspired to avoid using organic acid salts and Hirano et al. and Tsuruda et al. do not use organic acid salts in the fentanyl patches.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHANON A. FOLEY whose telephone number is (571)272-0898. The examiner can normally be reached on flex, generally M-F 7AM - 3 PM, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shanon A. Foley/
Primary Examiner
Art Unit 1619